RNA interference (RNAi) is an evolutionary conserved mechanism for controlling gene expression. The key elements in this process are a class of 19-25 bp double strand RNAs, collectively termed Small Interfering RNA (siRNA). RNAi was discovered only 13 years, but is nowadays considered a major potential pathway in non viral gene therapy. However, to make it a biomedical reality efficient delivery agents for siRNA must be designed. A large number nanovectors have been proposed and characterized, leveraging on the research developed these latest decades for DNA delivery. Here we describe the formation of complexes between a 21 bp siRNA which blocks the expression of hERG1 potassium channel (involved in the pathogenesis of several human cancers) and two types of dimeric cationic surfactants, i.e. trametya ammonium gemini with general formula (1) and a triazine-based surfactant (2)

Complementary techniques such as SANS, SAXS and DLS were used to investigate the structure and size of the obtained complexes, while charge evolution upon adding siRNA to micelles was followed by Zeta Potential. The kinetics of complex formation was studied by time-resolved synchrotron SAXS. A sigmoidal decrease of the surface charge was obtained for all surfactants at increasing siRNA content. The inflection point (i.e. neutrality) occurred at about \(-/+=1\), indicating that practically all the positive and negative charges were involved in the interaction. DLS measurements showed that the mean diameter of complexes was in the range 100-500 nm, except close to neutrality, where the aggregates had a markedly larger size (up to more than 1000 nm).

The analysis of scattering patterns allowed to describe these systems as being composed of internally structured coacervates, which nucleate from the micelle solution upon progressive siRNA addition. Modelling of the scattering patterns also allowed to establish an order of affinity between the investigated surfactants and siRNA. We believe that the wealth of information obtained in this study are a valuable pre-requisite to guide transfection experiments.